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ARMY ENVIRONMENTAL HYGIENE AGENCY ABERDEEN PROVING GR--ETC F/G 6/6  
TOPICAL HAZARD EVALUATION PROGRAM OF CANDIDATE INSECT REPELLENT--ETC(U)  
MAY 77 M H WEEKS, B J DESENA  
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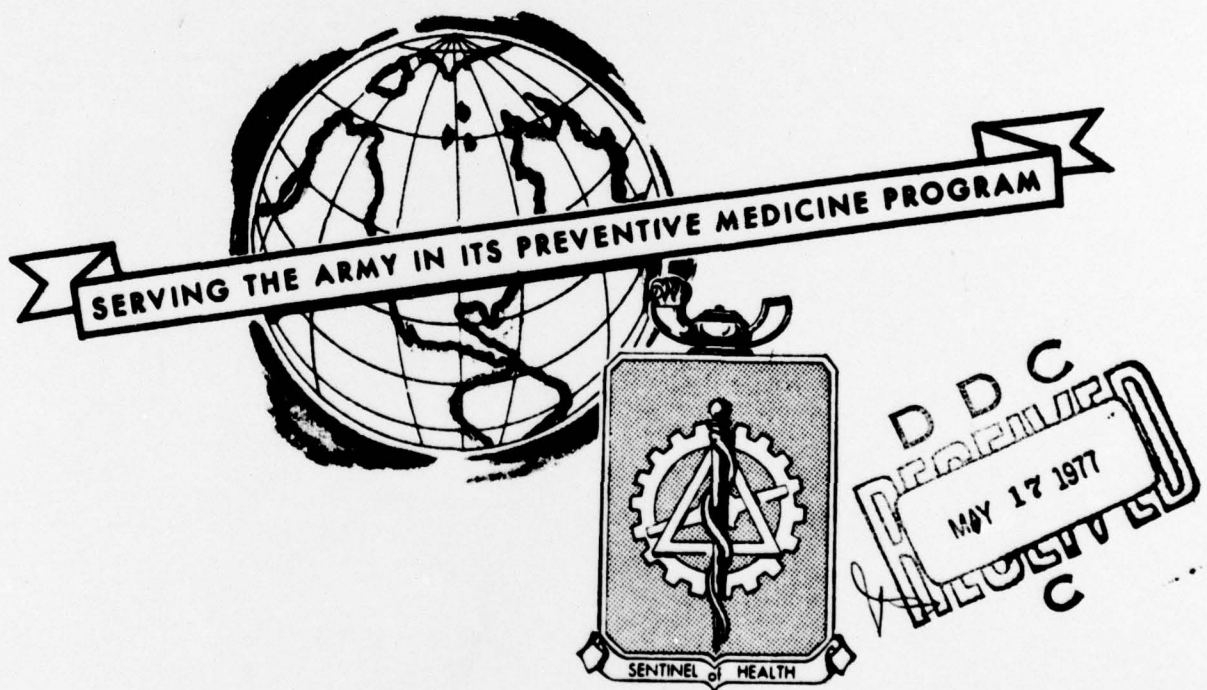


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TOPICAL HAZARD EVALUATION OF  
CANDIDATE INSECT REPELLENT AI3-36559  
4-METHYL-1-[(2-METHYLCYCLOHEXYL)CARBONYL]PIPERIDINE  
TOPICAL HAZARD EVALUATION PROGRAM  
STUDY NO. 51-0821-77  
OCTOBER 1975 - DECEMBER 1976



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ABERDEEN PROVING GROUND, MD 21010

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ABSTRACT (Continue on reverse side if necessary and identify by block number) A hazard evaluation of AI3-36559 was conducted using New Zealand White rabbits for skin and eye studies and Hartley guinea pigs for a skin sensitization study. Technical grade compound caused in rabbits moderate eye injury. Ethanol solutions of AI3-36559 caused primary skin irritation and may be irritating to the skin of man. Based on these findings, it is recommended that AI3-36559 not be approved for further testing as a candidate topical insect repellent. However, should the insect repellent qualities indicate that it presents a substantial improvement over standard repellents, it should be resubmitted in the form and concentration intended for usage.		

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DEPARTMENT OF THE ARMY  
U. S. ARMY ENVIRONMENTAL HYGIENE AGENCY  
ABERDEEN PROVING GROUND, MARYLAND 21010

12 MAY 1977

TOPICAL HAZARD EVALUATION OF  
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ABSTRACT

A hazard evaluation of AI3-36559 was conducted using New Zealand White rabbits for skin and eye studies and Hartley guinea pigs for a skin sensitization study. Technical grade compound caused in rabbits moderate eye injury. Ethanol solutions of AI3-36559 caused primary skin irritation and may be irritating to the skin of man. Based on these findings, it is recommended that AI3-36559 not be approved for further testing as a candidate topical insect repellent. However, should the insect repellent qualities indicate that it presents a substantial improvement over standard repellents, it should be resubmitted in the form and concentration intended for usage.

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ABERDEEN PROVING GROUND, MARYLAND 21010

TOPICAL HAZARD EVALUATION OF  
CANDIDATE INSECT REPELLENT AI3-36559  
4-METHYL-1-[(2-METHYLCYCLOHEXYL)CARBONYL]PIPERIDINE  
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1. AUTHORITY.

a. Letter, US Department of Agriculture, Agricultural Research Service, Southern Region, Insects Affecting Man Research Laboratory, Gainesville, FL, 17 October 1975.

b. Memorandum of Understanding Between the US Department of the Army, Office of The Surgeon General, the US Army Health Services Command, the US Army Environmental Hygiene Agency, the Armed Forces Pest Control Board and the US Department of Agriculture, effective December 1970 with Amendment No. 1, effective August 1974.

2. REFERENCE. Toxicology Division Procedural Guide, US Army Environmental Hygiene Agency (USAEHA), 1972.

3. PURPOSE. The purpose of this study was to provide guidance for further entomological testing of the candidate insect repellent AI3-36559.

4. SUMMARY OF FINDINGS. A hazard evaluation of the candidate repellent AI3-36559, 4-methyl-1-[(2-methylcyclohexyl)carbonyl]piperidine, was conducted by this Agency using New Zealand White rabbits for skin and eye studies and Hartley guinea pigs for a skin sensitization study. A tabular presentation of animal toxicity data developed in this Agency follows:\*†

\* In conducting the studies described in this report, the investigators adhered to the "Guide for the Care and Use of Laboratory Animals," US Department of Health, Education and Welfare, Publication No. (NIH) 74-23, revised 1972, second printing 1974.

† The experiments reported herein were performed in animal facilities fully accredited by the American Association for Accreditation of Laboratory Animal Care.

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Study No. 51-0821-77, Oct 75-Dec 76

TABULAR PRESENTATION OF DATA

Test	Results	Interpretation
<u>SKIN IRRITATION STUDIES</u>		
<u>Rabbits</u>		
Single 24-hr application to intact and abraded skin of New Zealand White rabbits.	AI3-36559 produced no primary irritation of the intact skin and only very slight erythema to abraded skin at 24 hr.	USAEHA Category I (reference Appendix)
0.5 ml technical grade compound applied to each of six rabbits.	No signs at 72 hr and 7 days.	
<u>EYE IRRITATION STUDIES</u>		
<u>Rabbits</u>		
Single 24-hr application 0.1 ml technical grade compound to one eye of each of six New Zealand White rabbits.	AI3-36559 produced mild injury to the cornea and moderate injury to the conjunctiva.	USAEHA Category E (reference Appendix)
	No signs at 7 days.	
<u>SENSITIZATION STUDIES</u>		
<u>Guinea Pigs (male)</u>		
Intradermal injection of 0.1 ml of a 0.1 percent suspension (w/v) of AI3-36559 or dinitro-chlorobenzene (DNCB)* in a mixture containing 1 volume of propylene glycol and 29 volumes of saline.		

\* A known skin sensitizer.



Study No. 51-0821-77, Oct 75-Dec 76

Test	Results	Interpretation
Ten test guinea pigs received and challenged with 0.1 percent suspension of AI3-36559.	Challenge dose of test compound (last intradermal injection) did not produce a sensitization reaction.	Compound AI3-36559 did not produce a sensitization reaction under test conditions and is not expected to produce a sensitization reaction in man.
Ten positive control guinea pigs received and challenged with 0.1 percent suspension of DNCB.	Positive control (DNCB) produced a marked sensitization reaction in 10 out of 10 guinea pigs.	
Ten cage control guinea pigs; five receiving challenge dose of test compound without prior sensitizing doses; five receiving challenge dose of DNCB without prior sensitizing doses.	Cage control guinea pigs showed no greater reaction to test compound and DNCB than was seen in original test groups.	

PHOTOCHEMICAL SKIN  
IRRITATION STUDIES  
Rabbits

A single application (0.05 ml) of 25-percent (w/v) solution of the compound and a 10-percent (w/v) oil of Bergamot solution (positive control) in 95 percent ethyl alcohol, were applied to the intact skin of six New Zealand White rabbits. Five minutes after application, the rabbits were exposed to UV light (365 nm) for 30 minutes from a distance of 10 to 15 cm.

AI3-36559 did not cause a photochemical skin irritation reaction under test conditions. However, ethanol solutions of AI3-36559 caused well-defined erythema and slight edema lasting 3 days at the nonirradiated skin sites. Moderate-to-severe erythema and edema was observed at the irradiated skin sites.

Although AI3-36559 was not a photochemical skin irritant, ethanol solution of this compound were primary skin irritants and may cause a similar skin reaction in man.

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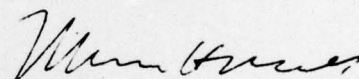
Following UV exposure of the rabbits, 0.05 ml of the test compound, positive control, and diluent were applied to additional skin areas to serve as unirradiated control sites.

Application areas were checked for irritation at

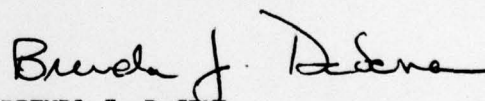
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5. CONCLUSION. Technical grade AI3-36559 caused moderate eye injury, as 25 percent solutions in ethyl alcohol skin irritation and may cause similar adverse reactions in man.

6. RECOMMENDATIONS. Under the provisions of the Memorandum of Understanding (reference paragraph 1b), it is recommended that AI3-36559, 4-methyl-1-[(2-methylcyclohexyl)carbonyl]piperidine not be approved for further testing as a candidate topical insect repellent. However, should the insect repellent qualities indicate that it presents a substantial improvement over standard repellents, it should be resubmitted in the form and concentration intended for usage.

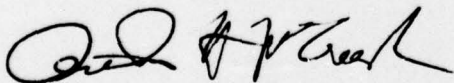


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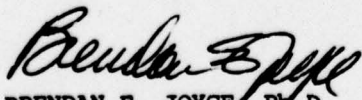


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## APPENDIX

### TOPICAL HAZARD EVALUATION PROGRAM DEFINITIONS OF CATEGORIES OF COMPOUNDS BEING CONSIDERED FOR ACUTE SKIN APPLICATIONS

CATEGORY I - Compounds producing no primary irritation of the intact skin or no greater than mild primary irritation of the skin surrounding an abrasion. (INTERPRETATION: No restriction for acute application to the human skin.)

CATEGORY II - Compounds producing mild primary irritation of the intact skin and the skin surrounding an abrasion. (INTERPRETATION: Should be used only on human skin found by examination to have no abrasions or may be used as a clothing impregnant.)

CATEGORY III - Compounds producing moderate primary irritation of the intact skin and the skin surrounding an abrasion. (INTERPRETATION: Should not be used directly on the skin without a prophetic patch test having been conducted on humans to determine irritation potential to human skin. May be used without patch testing, with extreme caution, as clothing impregnants. Compound should be resubmitted in the form and at the intended use concentration so that its irritation potential can be reexamined using other test techniques on animals, prior to human testing.

CATEGORY IV - Compounds producing moderate to severe primary irritation of the intact skin and of the skin surrounding an abrasion and, in addition, producing necrosis, vesiculation and/or eschars. (INTERPRETATION: Should be resubmitted for testing in the form and at the intended use concentration. Upon resubmission, its irritation potential will be reexamined using other test techniques on animals, prior to possible prophetic patch testing in humans, at concentrations which have been shown not to produce primary irritation in animals.)

CATEGORY V - Compounds impossible to classify because of staining of the skin or other masking effects owing to physical properties of the compound. (INTERPRETATION: Not suitable for use on humans.)

#### EYE CATEGORIES:

A. Compounds noninjurious to the eye. INTERPRETATION: Irritation of human eyes is not expected if the compound should accidentally get into the eyes, provided it is washed out as soon as possible.

B. Compounds producing mild injury to the cornea. INTERPRETATION: Should be used with caution around the eyes.

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C. Compounds producing mild injury to the cornea, and in addition some injury to the conjunctiva. INTERPRETATION: Should be used with caution around the eyes and mucosa.

D. Compounds producing moderate injury to the cornea. INTERPRETATION: Should be used with extreme caution around the eyes.

E. Compounds producing moderate injury to the cornea, and in addition producing some injury to the conjunctiva. INTERPRETATION: Should be used with extreme caution around the eyes and mucosa.

F. Compounds producing severe injury to the cornea and to the conjunctiva. INTERPRETATION: Should be used with extreme caution. It is recommended that use be restricted to areas other than the face.